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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,697	05/03/2005	Sylvain Rault	SERVIER 457 PCT	6150
25666 7590 03/05/2007 THE FIRM OF HUESCHEN AND SAGE SEVENTH FLOOR, KALAMAZOO BUILDING 107 WEST MICHIGAN AVENUE KALAMAZOO, MI 49007			EXAMINER JAISLE, CECILIA M	
			ART UNIT 1624	PAPER NUMBER
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		03/05/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/533,697

Applicant(s)

RAULT ET AL.

Examiner

Cecilia M. Jaisle

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-38,40 and 43-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 29-37 and 45 is/are allowed.
- 6) ☒ Claim(s) 38, 40, 43 and 44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application
- ☐ Other: _____.

DETAILED OFFICE ACTION

Rejections Under 35 USC 112

Claims 38, 40, 43 and 44 are again rejected under 35 USC 112, paragraph one, for reasons of record in the previous Office Action. The specification, while being enabling for specific compounds of Formula (I) as hypolipaemic agents (pages 12-13), does not provide reasonable enablement for the breadth of the claimed Formula (I) compounds for treating cancer in a living animal body. The following reasons apply.

The claimed compounds are shown to be hypolipaemic (hypolipidemic) agents in obesity-associated insulin resistant mice (page 12), however, the specification asserts that the claimed compounds are also useful to treat a living animal body afflicted with cancer, for which the specification provides no competent evidence. The specification provides no factual basis for the assertion that all of the claimed compounds treat all kinds of cancer and at all stages. The single test showing that the claimed compounds have hypolipaemic activity in obesity-associated insulin resistant mice (page 12) offers no evidence establishing any connection between treatment of hyperlipidaemia and treatment of any and all forms of cancer. The kinase screening (page 12) provides no identification of the specific kinases screened, the specific screening procedures used, no correlation between any specific compound of the present invention and a specific kinase, no correlation between any specific kinase activity and a specific cancer condition associated therewith, and no indication whether the individual tested compound exhibited a potentiating or inhibiting effect in regard to a specific kinase

Art Unit: 1624

activity. The On-line Medical Dictionary for the Centre for Cancer Education at the University of Newcastle-upon-Tyne defines kinase as an abbreviation for phosphokinase or phosphotransferase, which in turn is defined as simply an enzyme, a "protein molecule produced by living organisms that catalyses chemical reactions," having six main groups. There is no indication that the testing reported in the present specification is in any way commensurate in scope with the broadest meaning of kinase.

Claims 38, 40, 43 and 44 are drawn to treating cancer. A web cancer resource, <http://www.oncolink.com/types/index.cfm>, presents a detailed list of cancers. Perusal of the links to various cancer types there presented establishes various causes (if known) and varieties of treatment (if available) for each cancer type. The kinase screening in the specification, as discussed *supra*, fails to correlate a particular kinase with effective treatment of a particular cancer, let alone all of the cancers listed on OncoLink.

The medical literature, exemplified by Goueli, Gilbert, Rask-Madsen and Leng, all discussed in detail in the previous Office Action, supports that there is a specific empirically-determinable correlation between a kinase activity and a disease/condition; that the identification of an agent that modulates the activity of a specific kinase cannot support a generalized conclusion that that agent will alleviate kinase activity in regard to other diseases/conditions.

Many if not most cancers said to be treated by the claimed methods are known as difficult to treat. Although the present specification asserts that all of the claimed compounds modulate kinase activity, the only hypolipaemic activity is demonstrated. Substantiation of the method of use is required when utility is "speculative," "sufficiently

Art Unit: 1624

unusual" or not provided. See *Ex parte Jovanovics, et al.*, 211 USPQ 907, 909 (BPAI 1981). Also, note *Hoffman v. Klaus*, 9 USPQ2d 1657 (BPAI 1988) and *Ex parte Powers*, 220 USPQ 924 (BPAI 1982) regarding types of testing needed to support *in vivo* uses. The discussion of the individual *Wands* factors in the previous Office Action is repeated here in detail. The conclusion is that undue experimentation would be required to practice Applicants' invention. Proper limitation of claims 38, 40, 43 and 44 to a method for the control of hypolipaemia would be seen to overcome this rejection in regard to those claims.

Reply to Applicant's Response of Jan. 22, 2007

The Declaration by Dr. Sylvain Rault under 37 CFR 1.132 is insufficient to overcome the rejection of claims 38, 40, 43 and 44 based upon enablement of these claims under 35 USC 112, first paragraph, for treating a living animal body afflicted with cancer as set forth in the last Office Action for the following reasons. Initially, the Rault Declaration fails to state when the tests reported in Paragraph 8 thereof were carried out, so that issues related to prior public use under 35 USC 102(b) may be considered.

The specification must be enabling as of the filing date. MPEP §2164.05(a). Since the Rault Declaration is dated after the filing date of this application, it cannot be relied on to establish that the specification was enabling for the present claims as related to cancer treatment as of the filing date. Whether the specification would have been enabling as of the filing date involves consideration of the nature of the invention,

Art Unit: 1624

the state of the prior art, and the level of skill in the art. These issues were fully discussed in the previous Office Action under the consideration of the *Wands* factors.

Publications, such as Trevino and Summy, relied on in the Rault Declaration, also dated after the present filing date, provide information publicly first disclosed after the filing date and cannot be used to show what was known at the time of filing. *In re Gunn*, 190 USPQ 402,405-06 (CCPA 1976); *In re Budnick*, 190 USPQ 422, 424 (CCPA 1976) (stating that, if applicant seeks to use a publication to prove the state of the art for the purpose of the enablement requirement, the publication must have a publication date earlier than the effective filing date of the application). A later dated publication cannot supplement an insufficient disclosure in a prior dated application to make it enabling. *Gould v. Quigg*, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987).

Since a *prima facie* case of lack of enablement has been established for claims 38, 40, 43 and 44 for treating any living animal body afflicted with any form of cancer at any stage, Applicants' burden is to present persuasive arguments, supported by suitable proofs where necessary, that one skilled in the art at the time this invention was made would have been able to use the claimed invention. *In re Brandstadter*, 179 USPQ 286 (CCPA 1973). Because this specification on its face appears deficient under 35 U.S.C. 112, first paragraph, any supplemental evidence must establish that the information which must be read into the specification to make it complete would have been known to those of ordinary skill in the art at the time this invention was made, i.e., as of the filing date of this application. MPEP §716.09. The Rault Declaration presents no such evidence.

Applicants are not precluded from providing a Rule 132 declaration or affidavit after the filing date that demonstrates that the claimed invention works. However, a careful comparison of the steps, materials and conditions reported in the Rault Declaration, especially in Paragraph 8 thereof, with those disclosed in the application reveals that the specification and the Rault Declaration are not at all commensurate in scope. The specification (page 12) fails to identify the "conventional screening methods" and "commercially available kinases" or the nature of the activating, inhibiting and potentiating properties observed for the compounds of present Formula (I). The Rault Declaration fails to identify the "conventional screening methods" used and fails to establish that they are the same as the "conventional screening methods" mentioned in the specification. The Rault Declaration tests the compound of example 7 in regard to Src kinases, but fails to establish that Src kinases are the same as the "commercially available kinases" mentioned in the specification. As noted in the previous Office Action, the On-line Medical Dictionary for the Centre for Cancer Education at the University of Newcastle-upon-Tyne defines "kinase" as a phosphokinase or phosphotransferase, which in turn is defined as an enzyme, a "protein molecule produced by living organisms that catalyses chemical reactions," having six main groups. There is no substantiation that the kinase alluded to in the present specification is specifically the Src kinase reported in the Rault Declaration. MPEP 2164.05

The Federal Circuit found lack of enablement in *Enzo Biochem, Inc. v. Calgene, Inc.*, 52 USPQ2d 1129 (Fed. Cir. 1999). There, the court held invalid claims in two patents directed to genetic antisense technology (which aims to control gene expression

in a particular organism), because the breadth of enablement was not commensurate in scope with the claims. The specifications disclosed applying antisense technology in regulating three *E. coli* genes. The specifications' limited disclosures asserted, "[t]he practices of this invention are generally applicable with respect to any organism containing genetic material which is capable of being expressed ... such as bacteria, yeast, and other cellular organisms." The patent claims encompassed application of antisense methodology in a broad range of organisms. The court relied on the facts that (1) the amount of direction presented and number of working examples provided in the specification were narrow compared to the breadth of the claims at issue, (2) antisense gene technology was highly unpredictable, and (3) the amount of experimentation required to adapt the creation of antisense DNA from *E. coli* to other types of cells was quite high, especially since the record included examples of the inventor's failures to control expression of other genes in *E. coli* and other types of cells. The specification was found to offer only a "plan" or "invitation" for those of skill in the art to experiment using the technology in other cell types.

By analogy, in the present fact situation, the breadth of enablement is not commensurate in scope with the claims to a "method for treating a living animal body afflicted with cancer." Here, the specification (page 12) provides nebulous, illdefined directions that cannot be termed a "working example." The treatment of cancer is highly unpredictable. The OncoLink, cited *supra*, reports the wide range of cancers and treatments therefor. A review of the current literature substantiates the inability of researchers to locate a single therapy treatment for all types of cancers. Walsh, BBC

Art Unit: 1624

News, International Version, Medical Notes, Feb. 1, 2007, quotes Prof. Fiona Watt,

"We've known for many years that not all tumour cells are the same." PharmaLicensing

(Mar. 2005), reviewing a number of commercially available cancer treatments, reports:

Effective cancer therapies are focused on the development of agents capable of selectively destroying tumour cells while sparing normal tissues. With this aim, major efforts have been directed at harnessing the specificity of the immune response. The discovery of hydridoma technology in the 1970s enabled the development of tumour-selective monoclonal antibodies (MAbs), creating a targeted therapeutic approach resulting in the selective death of cancer cells. ... Despite the success of currently marketed cancer MAb therapies, however, the dream of a 'magic bullet' of antibody therapy has remained elusive.

Regarding application of point (2) of *Enzo Biochem* to the present situation, treatment of all types of cancer with a single agent remains highly unpredictable, as borne out by Walsh and PharmaLicensing discussed *supra*. Even with regard to inhibition of Src kinase, Serrels, et al., Mol. Cancer. Ther., 2006, 5 (12), Dec. 2006, report, "concentrations of dasatinib [an orally active, multi-targeted kinase inhibitor that targets Src family kinases, under clinical evaluation for solid tumor treatment] that inhibit Src activity do not inhibit proliferation in 10 of 12 colon cancer cell lines."

Regarding application of point (3) of *Enzo Biochem* to the present situation, the amount of experimentation required to determine which of the present Formula (I) compounds were be effective for the treatment of which types of cancer would be quite high, especially since the record included no working examples and the literature (Walsh, PharmaLicensing) establishes the failure of researchers to identify a single effective treatment for all forms of cancer and Serrels establishes the inability of Src inhibitors to control all forms of even a single cancer, colon cancer.

Art Unit: 1624

Proper limitation of claims 38, 40, 43 and 44 to a method for the control of hypolipaemia would be seen to overcome this rejection in regard to those claims. Otherwise, this rejection is made FINAL.

Conclusion

Claims 1-28, 39, 41 and 42 are canceled. Claims 29-38, 40 and 43-45 are pending. Claims 29-37 and 45 are allowable. Claims 38, 40, 43 and 44 are rejected and this rejection is made FINAL.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cecilia M. Jaisle, J.D. whose telephone number is 571-272-9931. The examiner can normally be reached on Monday through Friday; 8:30 am through 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1624

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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